PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
MIC-017 PCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/EP2004/013445	26/11/2004	28/11/2003
Applicant		
MICROMET AG		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 9 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
      [ ] The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. [X] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [X] **Certain claims were found unsearchable** (See Box II).

3. [X] **Unity of invention is lacking** (see Box III).

4. With regard to the **title,**
   [X] the text is approved as submitted by the applicant.
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   [X] the text is approved as submitted by the applicant.
   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. _____
      [ ] as suggested by the applicant.
      [ ] as selected by this Authority, because the applicant failed to suggest a figure.
      [ ] as selected by this Authority, because this figure better characterizes the invention.
   b. [X] none of the figures is to be published with the abstract.

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International application No.
PCT/EP2004/013445

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. type of material

   [X] a sequence listing

   [ ] table(s) related to the sequence listing

   b. format of material

   [X] in written format

   [X] in computer readable form

   c. time of filing/furnishing

   [X] contained in the international application as filed

   [X] filed together with the international application in computer readable form

   [ ] furnished subsequently to this Authority for the purpose of search

2. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

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International application No.
PCT/EP2004/013445

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 20,22-25 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [X] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[X] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-4,19-25 (all completely)

bispecific antibody and therapeutic use

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2. claims: 5-18 (all completely)

method for producing a bispecific antibody that binds CD3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/013445

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K39/395 C07K16/28 · C07K16/46

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 348 715 A (MICROMET AG) 1 October 2003 (2003-10-01) the whole document	1-25
X	LOEFFLER A ET AL: "Efficient elimination of chronic lymphocytic leukaemia B cells by autologous T cells with a bispecific anti-CD19/anti-CD3 single-chain antibody construct" LEUKEMIA, MACMILLAN PRESS LTD, US, vol. 17, no. 5, May 2003 (2003-05), pages 900-909, XP002299902 ISSN: 0887-6924 the whole document	1-4, 19-25

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 October 2005	04 11 2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Gruber, A

Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LOEFFLER ANJA ET AL: "A recombinant bispecific single-chain antibody, CD19 X CD3, induces rapid and high lymphoma-directed cytotoxicity by unstimulated T lymphocytes" BLOOD, W.B.SAUNDERS COMPANY, ORLANDO, FL, US, vol. 95, no. 6, 15 March 2000 (2000-03-15), pages 2098-2103, XP002299904 ISSN: 0006-4971 the whole document	1-4,19
X	SCHOBERTH A ET AL: "A new class of trifunctional bispecific antibodies mediated efficient immunological purging of peripheral blood stem cells" EUROPEAN JOURNAL OF CANCER, PERGAMON PRESS, OXFORD, GB, vol. 37, September 2001 (2001-09), page S51, XP004381555 ISSN: 0959-8049 the whole document	1,19-22
X	JAGER M ET AL: "Immune monitoring of tumor cell elimination from malignant ascites during immunotherapy with trifunctional bispecific antibodies" EUROPEAN JOURNAL OF CANCER, PERGAMON PRESS, OXFORD, GB, vol. 37, September 2001 (2001-09), page S60, XP004381568 ISSN: 0959-8049 the whole document	1,19-22
X	WO 99/54440 A (DOERKEN, BERND; RIETHMUELLER, GERT; KUFER, PETER; LUTTERBUESE, RALF; B) 28 October 1999 (1999-10-28) the whole document	1-4, 19-25
X	MALETZ K ET AL: "Bispecific single-chain antibodies as effective tools for eliminating epithelial cancer cells from human stem cell preparations by redirected cell cytotoxicity" INTERNATIONAL JOURNAL OF CANCER, NEW YORK, NY, US, vol. 93, no. 3, 1 August 2001 (2001-08-01), pages 409-416, XP002301955 ISSN: 0020-7136 the whole document	1,19

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	HOFFMANN PATRICK ET AL: "Serial killing of tumor cells by cytotoxic T cells redirected with a CD19-/CD3-bispecific single-chain antibody construct." INTERNATIONAL JOURNAL OF CANCER. JOURNAL INTERNATIONAL DU CANCER. 20 MAY 2005, vol. 115, no. 1, 20 May 2005 (2005-05-20), pages 98-104, XP002335808 ISSN: 0020-7136 the whole document	1-4, 19-25
A	LUELLAU E ET AL: "Development of a downstream process for the isolation and separation of monoclonal immunoglobulin A monomers, dimers and polymers from cell culture supernatant" JOURNAL OF CHROMATOGRAPHY A, ELSEVIER, AMSTERDAM, NL, vol. 796, no. 1, 13 February 1998 (1998-02-13), pages 165-175, XP004108678 ISSN: 0021-9673 page 166, left-hand column, paragraph 1 - paragraph 2	1-25
A	KRETZSCHMAR T ET AL: "High-level expression in insect cells and purification of secreted monomeric single-chain Fv antibodies" JOURNAL OF IMMUNOLOGICAL METHODS, ELSEVIER SCIENCE PUBLISHERS B.V.,AMSTERDAM, NL, vol. 195, no. 1, 9 September 1996 (1996-09-09), pages 93-101, XP004021258 ISSN: 0022-1759 page 94, left-hand column, paragraph 4	1-25
A	LEE Y C ET AL: "Reversible Dimer Formation and Stability of the Anti-tumour Single-chain Fv Antibody MFE-23 by Neutron Scattering, Analytical Ultracentrifugation, and NMR and FT-IR Spectroscopy" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 320, no. 1, 28 June 2002 (2002-06-28), pages 107-127, XP004449713 ISSN: 0022-2836 page 108, right-hand column, paragraph 2 page 121, right-hand column, paragraph 3	1-25

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WORN A ET AL: "Stability engineering of antibody single-chain Fv fragments" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 305, no. 5, 2 February 2001 (2001-02-02), pages 989-1010, XP004465987 ISSN: 0022-2836 page 995, right-hand column, paragraph 4	1-25
A	ARNDT K M ET AL: "Factors influencing the dimer to monomer transition of an antibody single-chain Fv fragment." BIOCHEMISTRY. 15 SEP 1998, vol. 37, no. 37, 15 September 1998 (1998-09-15), pages 12918-12926, XP002348237 ISSN: 0006-2960 page 12918, right-hand column, paragraph 2 page 12919, left-hand column, paragraph 2 page 12925, right-hand column, paragraph 2	1-25

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP2004/013445

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
EP 1348715	A	01-10-2003	EP	1071752 A1	31-01-2001
			SI	1071752 T1	31-12-2003
WO 9954440	A	28-10-1999	AT	244758 T	15-07-2003
			AU	761587 B2	05-06-2003
			AU	4135299 A	08-11-1999
			BG	104868 A	28-09-2001
			BR	9909860 A	19-12-2000
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			DE	69909459 T2	27-05-2004
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			PL	344016 A1	24-09-2001
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			RU	2228202 C2	10-05-2004
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